



Research Paper: The Relationship Between Serum Dehydroepiandrosterone Concentration and Memory Function in the Elderly



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Running Title Dehydroepiandrosterone (DHEA) and Memory

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ABSTRACT

Background: World population is rapidly aging, and the elderly are most at risk of cognitive impairment. Dehydroepiandrosterone (DHEA) and DHEA-Sulfate (DHEAS) have an essential effect on neuroprotection and might effectively improve cognition and memory.

Objectives: This study aimed to investigate the relationship between the level of DHEA and memory function in the elderly.

Materials & Methods: The present study was a cross-sectional analytical study, and the study population included the elderly (age 60 years and older) living in Rasht City, the north of Iran, in 2020. The participants completed a demographic questionnaire and Wechsler Memory Scale (WMS), and their serum DHEA levels were measured by the hormonal automation method. The data were analyzed by SPSS v. 23, using t-test, the one-way Analysis of Variance (ANOVA), Pearson and Spearman correlation coefficient.

Results: The participants included 100 older people (57 females and 43 males) with a Mean±SD age of 67.38±5.39 years. There was no correlation between serum DHEA concentrations with a total score of the WMS ($r=0.117$, $P=0.247$). However, the correlation between the DHEA level and the scores of personal and current information and visual reproduction subscales were statistically significant ($r=0.219$, $P=0.029$; $r=0.206$, $P=0.04$).

Conclusion: The study indicates that the total memory score was not associated with the level of serum DHEA.

Keywords: Dehydroepiandrosterone, Memory, Wechsler Memory Scale

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Highlights

- According to this study, the total memory score was not associated with the level of serum Dehydroepiandrosterone (DHEA).
- Personal and current information and visual reproduction were associated with the DHEA concentration level.

Introduction

Dehydroepiandrosterone (DHEA) and its sulfate ester (DHEAS) are the most abundant steroid hormones in humans, produced by the zona reticularis of the adrenal cortex [1]. The level of DHEA begins to rise at ages 6–8 years, a phenomenon called “adrenarche”. DHEA levels peak during the third decade of life and then gradually decrease over time in both men and women [2]. Its serum concentrations decrease 20% less than their peak, at approximately 65 to 70 years. Around this time, many age-related illnesses may occur [1].

According to studies, neurosteroids regulate various brain functions, such as cognition, stress, depression, anxiety, sleep, and sexual- and feeding-related behaviors and locomotion [3, 4]. DHEA has modulatory actions on the Central Nervous System (CNS), and it is also called neuroactive steroid [5]. Also, DHEAS is known for its antioxidant properties and ability to help neuronal protection [6]. Decreasing DHEA level with increasing age may be associated with brain aging, aging-related neurodegeneration, and gradual cognitive decline [7] by influencing synaptic connectivity and neuronal differentiation [3].

The world’s population is rapidly aging, so meeting the needs and problems of this age group is a social necessity [8]. Both biological and psychological changes occur with aging [9]. Older people have the highest risk of cognitive impairment [8]. The essential components of cognition include perception, learning, memory, attention, and vigilance. Memory is a function that gives meaning to time and requires several successive stages [6]. Memory or cognitive impairment can decline daily activities. In the mild form, individuals in simpler activities retain independence, but in the severe forms doing basic activities of daily life is compromised [10]. So, impairment of memory and other cognitive domains is the leading cause of functional dependence, poor quality of life, and mortality in the elderly [9]. On the other hand, cognitive impairment has a financial and psychological burden on individuals, caregivers, and society [11].

Most cognitive impairment occurs in over 60 years old, and about 32% occurs at the age above 85 years [12]. Therefore, it is crucial to prevent or slow down the process of cognitive impairment. Decreased cognitive ability simultaneously as decreased DHEA levels hypothesize the relationship between the two [13]. According to the results of studies, decreased DHEAS concentrations may be an essential indicator for Alzheimer disease [14], and it is beneficial for improving memory [15]. However, the studies have found contradictory results about the relationship between DHEAS concentrations and cognitive function in the elderly [1, 14, 16].

Although a systematic review of the studies investigating the role of DHEA and DHEAS in Alzheimer disease showed their involvement in the pathophysiology of the disease [17], the results of the studies on the general population without severe cognitive impairment showed contradictory results. Elpers et al. examined the relationship between DHEAS and cognitive performance, and a positive correlation was found at baseline between DHEAS level and cognition in men, but not in women. Finally, they concluded that higher levels of DHEAS in older men were associated with cognitive levels but were unlikely to play a functional role in reducing cognition [16]. In another research on elderly African American women, the results showed that the increased levels of DHEA were associated with impaired psychomotor function, but they were not related to executive function [18]. In contrast, Vieira-Marques et al. showed that DHEA protects neurons against glucose deprivation in human neuroblastoma cells, which is correlated with cognitive performance [19]. Also, the results of one study indicated that DHEAS is positively associated with executive function and memory [20]. After investigating 295 healthy women (aged 21-77 years), it was found that executive function, working memory, and concentration were positively correlated with DHEAS concentrations (independent of age) [21]. Furthermore, a review of cross-sectional and longitudinal studies showed direct associations between DHEAS blood levels and global cognition in females and males, but direct relationships between DHEAS and working memory, attention, and verbal fluency were reported only in females [6].

Decreased DHEAS levels in old age and its coincidence with the increasing prevalence of cognitive impairment and considering the possible neuroprotective effect of DHEAS suggests a direct relationship between them. Because of the contradictory results in various studies, this issue has not been proven yet. Therefore, in the present study, we intend to investigate the relationship between DHEA levels and memory function in the elderly.

Materials and Methods

The present study is a cross-sectional analytical study, and the study population comprised the elderly (age 60 years and older) of Rasht City Retirement Organization (place of sampling), Iran, in 2020. After obtaining permission from the Ethics Committee at the Research Center of Guilan University of Medical Sciences (Ethics Code: IR.GUMS.REC.1398.217), 100 older men and women were selected by convenience sampling method. The inclusion criteria were old age, literacy for writing and reading, and willingness to participate in the study. The exclusion criteria were having serious psychiatric problems based on a psychiatric interview performed by researchers. After explaining the objectives of the project and obtaining informed consent, the participants completed a demographic information questionnaire and Wechsler Memory Scale (WMS), and then their serum DHEA concentration was measured.

Study tools

Demographic information questionnaire: This questionnaire was used for measuring demographic information, including age, sex, and level of education.

Wechsler Memory Scale (WMS): Wechsler introduced this scale in 1945. The original form of this scale was used in the present study that has seven subscales: personal and current information (0-6), orientation (0-5), mental control (0-9), logical memory (0-23), digit span (0-15), visual reproduction (0-14), and associative learning (0-21) [22]. The total sum of the subscales' scores is added to the fixed score of different age groups to obtain the corrected score. Finally, the memory score is determined based on the corrected score. In the Ryan et al. study, the reliability of this scale was 0.75 in normal individuals and 0.89 in patients with psychiatric disorders [23]. Sarrami measured the construct validity and face validity of this scale. For construct validity, factor analysis and internal consistency were done. According to factor analysis results, there were three final factors (logical memory, visual reproduction, and digits span). In the construct validity, there was a significant correla-

tion between each item of the test ($P=0.001$), and associative learning had a higher correlation with the total score of memory. Also, according to the measurement of face validity, there was a direct relationship between associative learning and memory score, and visual reproduction had high face validity. The reliability of the test using the alpha coefficient was 0.85 [24].

Statistical analysis

Assuming the alpha error of 0.05, the power of 0.20, and r of 0.25, the sample size was calculated 100 based on the study by Davis et al. [21]. After collecting the data, they were analyzed by SPSS v. 23. The observed data were described as Mean \pm SD, frequency, and percentage. For quantitative variables, t-test and the one-way Analysis of Variance (ANOVA) were used. The correlation relationships were examined by the Pearson correlation coefficient and Spearman correlation coefficient. The significance level was considered less than 0.05.

Results

In this study, 100 older adults with a Mean \pm SD age of 67.38 \pm 5.39 years participated. The subjects include both females (57%) and males (43%), in the two age groups of 60-70 years (71%) and over 70 years (29%). Their education degrees were as follows: less than diploma (21%), diploma (35%), undergraduate (14%), graduate (24%), and postgraduate (6%).

The comparison of serum DHEA concentrations in terms of sex and age of subjects by t-test indicated that males had a higher level of DHEA (101.29 \pm 71.89) than females (64.45 \pm 41.36), and the difference was statistically significant ($t=3.006$, $P=0.004$), while this difference was not significant between two age groups of the subjects ($t=0.436$, $P=0.664$).

There was no correlation between serum DHEA concentration and the age of the elderly using the Pearson correlation coefficient ($P=0.561$) (Figure 1). Table 1 indicates no statistically significant difference between the mean WMS in terms of sex and age of subjects ($P=0.731$, $P=0.652$), while this difference was statistically significant in terms of the level of education ($P=0.0001$).

A positive correlation was observed between WMS and the level of education, using the Spearman correlation coefficient-test ($P<0.001$) (Figure 2). According to the results, there is no correlation between serum DHEA concentration and the total scores of WMS ($P=0.247$), while the correlation between the

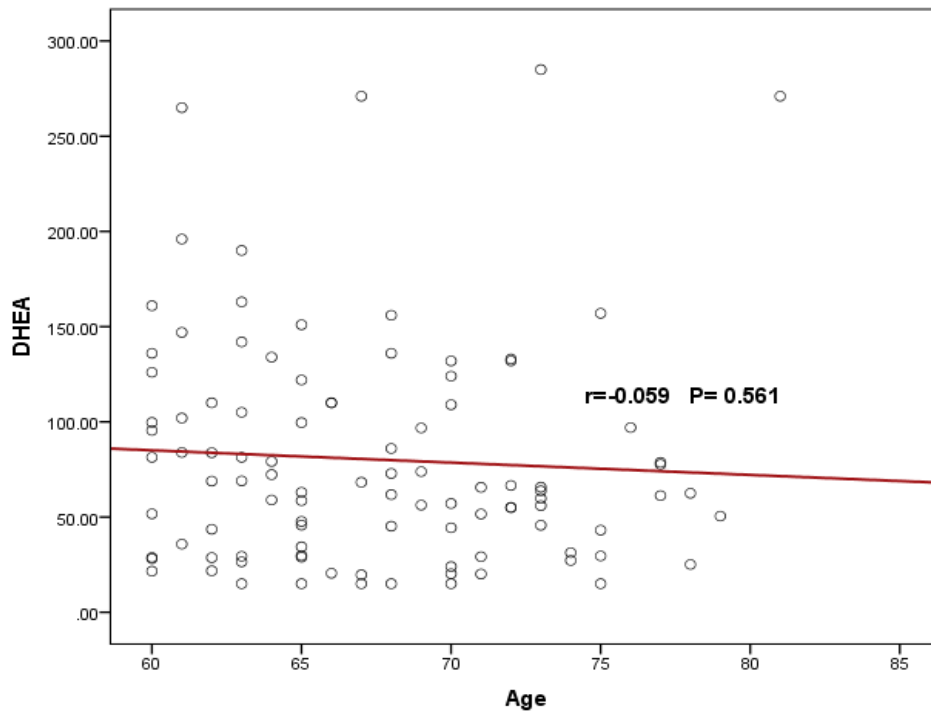


Figure 1. Correlation between Dehydroepiandrosterone (DHEA) and age



subscales of personal and current information and visual reproduction is statistically significant ($P=0.029$, $P=0.04$) (Table 2).

Discussion

In the present study, the relationship between serum DHEA concentration and memory function in the elderly was investigated in 100 older people (57 women

and 43 men) with a Mean±SD age of 67.38±5.39 years. The level of DHEA was significantly higher in males but, there was no significant relationship between serum DHEA concentration and the age of the elderly. Also, memory scores had no difference in terms of sex and age of subjects, while it was associated with the level of education, and participants with higher education had better memory scores. There was no relationship between serum DHEA concentration and total memory scores, but

Table 1. Comparison of Wechsler Memory Scale (WMS) and demographic variables

	Variables	n	WMS (Mean±SD)	Test Statistic	P
Sex	Female	57	56.60± 8.12	0.345	0.731*
	Male	43	56.02±8.35		
Age (y)	60-70	71	56.11±8.81	0.452	0.652*
	>70	29	56.93±6.50		
Educational level	< Diploma	21	50.86±7.83	6.590	0.0001**
	Diploma	35	56.51±7.06		
	Undergraduate	14	54.71±5.89		
	Graduate	24	62.00±7.64		
	Postgraduate	6	55.83±9.70		

*t-test,**One-way ANOVA.



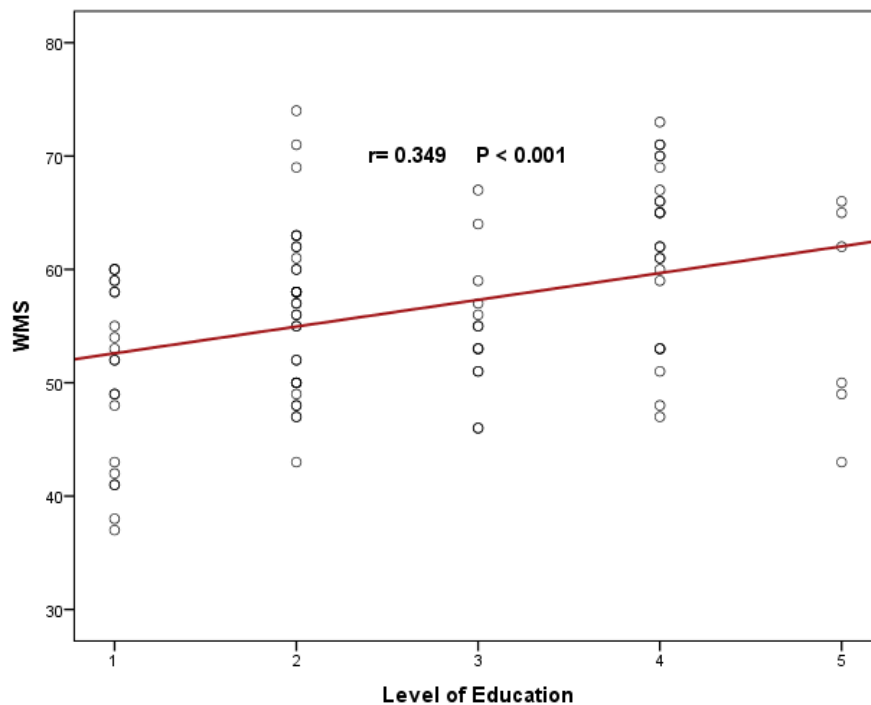


Figure 2. The correlation between Wechsler Memory Scale (WMS) and level of education



personal and current information and visual memory had a positive relationship with the level of DHEA. Consistent with the present study, most studies reported higher DHEAS levels in men than in women [21], but some studies found that the level of this hormone was higher in females [25, 26]. Because of these different results, a review study reported that sex difference in DHEAS levels is not clear [6].

The results of a cross-sectional study by Davis et al. on active African American older women are consistent with the present study that age was not related to DHEA results [18]. However, in another study on different age groups, DHEAS levels were negatively related to age [25]. Because of the gradual decline in hormone levels in each decade, the evaluation of a sample in an age group may not correctly show the decrease in hormonal levels resulting from apoptosis of cells in the adrenal reticular region [27].

Likewise, Ji-Hae et al. showed that the memory score was lower in the group with the lowest education than in

the highest education [28]. Also, Ahn et al. reported that low education was significantly associated with the low performance of the elderly in the memory test, and there was no difference in the memory performance in terms of sex [29]. This finding is consistent with our results.

According to the findings, in the memory test, the elderly had the best performance in the subscale of orientation to time and place with the mean value of 98.4% and the weakest performance in the logical memory subscale with the mean value of 32.43%. Because the study samples could independently manage their daily activities, answering the questions of the orientation subscale, i.e., about information and place, was not difficult for them. However, performing the logical memory subscale, memorizing the stories, and recalling them, were more challenging for them, and they scored lower overall.

Some studies reported a positive relationship between the level of DHEA and cognitive performance [6, 19-21, 30]. Hildreth et al. studied the association between

Table 2. Correlation between Dehydroepiandrosterone (DHEA) and Wechsler Memory Scale (WMS) and its subscales

The Pearson Correlation	Personal and Current Information	Orientation	Mental Control	Logical Memory	Digit Span	Visual Reproduction	Associative Learning	Total WMS
r	0.219	0.021	-0.145	0.042	0.046	0.206	0.113	0.117
p*	0.029	0.837	0.149	0.676	0.648	0.040	0.264	0.247

*The Pearson correlation.



serum DHEAS and three aspects of cognition: executive function, functional memory, and processing speed [31]. Their results showed that higher serum DHEAS levels were associated with better working memory and executive function in men [31]. In another research in 2020, a positive correlation between the level of DHEA and cognition was found in men, but the longitudinal investigation showed that the DHEA level did not affect cognitive decline [11]. Also, a systematic review of the studies found little evidence supporting the effect of DHEA on the treatment of Alzheimer disease [12].

One of the limitations of this study was that the participants were mainly from the same socio-economic status and lived in the city. In addition, the sampling was performed in retirement centers, and people referring to these centers usually have an appropriate general and cognitive function and could do their daily activities independently. In other words, this study was performed in the elderly with proper cognitive health.

Conclusion

The present study showed no differences in memory function in terms of sex and age, while participants with higher education had better memory function. The level of DHEA and total memory scores had no association. Consequently, we did not find any relationship between global memory and DHEA levels, but personal and current information and visual reproduction had a positive relationship with the level of DHEA.

Ethical Considerations

Compliance with ethical guidelines

The study was approved by the Ethics Committee of Guilan University of Medical Sciences (Ethical Code: IR.GUMS.REC.1398.217). All study procedures were done in compliance with the ethical guidelines of the Declaration of Helsinki, 2013.

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Authors' contributions

Conceptualization, investigation, writing the original draft, review, and editing: All authors; Methodology and supervision: Elahe Abdollahi and Robabeh Soleimani; Formal analysis: Golsa Olia, Fatemeh Eslamdoušt-Si-

ahestalkhi; Funding acquisition: Elahe Abdollahi; Data collection: Golsa Olia.

Conflict of interest

The authors declared no conflict of interest.

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